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Phytotherapeutic mechanism of medicinal plants with wound-healing potential: a mini-review

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Graphical Abstract

Abstract

The applications of medicinal plant species for diverse therapeutic effects are well documented throughout the world. In recent times, the screening of higher plants for unique biologically active compounds, particularly those with pronounced therapeutic potency, has received the interest of the science community. A wound is a loss or breaks in the anatomic stability of active tissue. It not only poses a physical and mental threat to zillions of people but could cause the failure of multiple organs, amputation, and even death. Therefore, thousands of plants have been screened to obtain active metabolites or compounds that can accelerate the process of restoring the damaged tissue structure and inhibit the probability of infections. Due to the severity of wounds to the human body, it is essential to explore safe, economical, and environmentally friendly therapeutics from nature. This review aims to conduct a comprehensive search of medicinal herbs to uncover their therapeutic potential, identify gaping holes, and assess future research prospects that could lead to the discovery of novel pharmacophores. Thus, the review is tailored towards the appraisals of phytotherapeutic mechanism and wound healing efficacy of medicinal plants, which will help spur future research and improve our current knowledge leading to the unearthing of novel and potent pharmacophores with pronounced wound healing potentials. Several medicinal plants with scientifically proven wound-healing activities are reported and discussed alongside phytochemicals present their various extracts and isolates. The achievable wound-healing closure rate of each plant was also reported with a focus on what is responsible for the healing rate.

Keywords: Wound; medicinal plant; secondary metabolites; therapeutic potency, healing mechanism.

1.0 Introduction

Wounds refer to the anatomical or physical disruptions caused by tearing, breaking, piercing, or cutting the skin epithelium and could be associated with connective tissue loss (Lordani *et al.*, 2018). It represents an important global healthcare challenge due to the high cost and inept therapeutic agents in managing wounds (Agyare *et al.*, 2016). In recent times, the impulse to search or explore potent wound therapeutics by researchers is voracious. Most of these researches are tailored towards unearthing innovative pharmacophores with the primary target of enhancing wound healing and also eradicating aftermath consequences. Traditional medicine has received long-standing interest since time immemorial as the major healthcare delivery system, especially in developing countries (Pei, 2001; Edewor *et al.*, 2015). It is also documented as the foremost medical care is known and is gaining more ground in both emerging and industrialized countries because it is safe, cost-effective, and eco-friendly, coupled with no side effects (Oladeji *et al.*, 2020a). The exploit of herbal drugs in primary health care is considered the oldest therapeutic system since the inception of man. According to the World Health Organization (WHO), herbal medicine is an alternative pathway in combating diseases and infections (WHO, 2016). Herbs are therapeutic constituents obtained from nature to treat various acute and chronic diseases (Kayser *et al.*, 2003).

The scientific approach has piloted the discovery of chemotherapeutic substances which have effectively inhibited plasmodium development, targeting the parasites at the blood stage of their life cycle. Several pharmacophores such as quinine (QN) were discovered in the nineteenth century and showed strong inhibitory activities against plasmodium species. However, at the arrival of synthesized drugs, plants and plant parts are used as drugs contracted. Unfortunately, as the use of synthesized drugs amplified, there was also an upsurge in resistance to the synthesized drugs by microbes, joined with the lethal nature of the drugs. Moreover, individuals respond to some of these drugs in different ways. These drawbacks of synthesized drugs triggered man to turn back to his genesis drugs source (plants) for his primary healthcare delivery, and this has brought about the use of an enormous number of medicinal plants with curative properties to treat several diseases (Oladeji *et al.*, 2021; Edewor *et al.*, 2015). The therapeutic actions of plants have been ascribed majorly to the secondary metabolites present in them (Fabeku, 2006). In addition, phytomedicine has shown outstanding potential in managing contagious ailments (Yesilada, 2005). Therefore, great attention has been given to the uses of plants and plant products, especially in those regions with no or slight access to new health facilities (Pei, 2001). Traditional healers were compelled to use any natural

substance to ease their pains, instigated by acute and chronic ailments, physical discomforts and wounds, and deadly infections (Yesilada, 2005).

However, the present phytochemical research is insufficient to support the use of plants as possible wound healers. As a result, this review is geared toward conducting a comprehensive search of medicinal herbs to uncover their therapeutic potential, identify gaping holes, and assess future research prospects that could lead to discovering novel pharmacophores.

2.0 Research methodology

This review was based on a comprehensive review of publicly available literature using major scientific databases such as SciFinder, Scopus, PubMed, Google Scholar, and Science Direct. The keywords utilized to scoop up the scientific journals were: wounds, traditional uses of plants, pharmacological activities of medicinal plants with wound healing potentials. Around 100 published papers were gathered with major focus on work done in the past 10 years and papers that were not written in English (15) or published before 2000 (26) were removed from the repository of publications downloaded.

3.0 Wounds and wound healing mechanism

The wound does not only affects the physical and psychological well-being of zillions of patients but also inflict a substantial cost on them, and recent evaluations show that about 6 million people are suffering from chronic wounds, which may even lead to failure of multiple organs and even death (Kumar *et al.*, 2007). According to the Wound Healing Society, Wounds are physical injuries that result in an opening or fracturing of the skin, interrupting normal skin biomechanical operation and possibly resulting in epithelium loss with or without impairment to the core connective tissue (Strodtbeck, 2001). The healing of a wound is a continuous process of three uninterrupted and over-lapping stages encompassing restoring normal structure and functions of damaged tissue or a survival mechanism that characterizes an attempt to maintain the normal anatomical structure (Lenselink 2015; Puratchikody *et al.*, 2006). Though wound healing is an acquainted process, its fundamental biology is complex and moderately stopped because unhealed wounds frequently develop inflammatory intermediaries that bring forth soreness and puffiness at the wound location (Sherratt and Dallon, 2002; Roberts *et al.*, 1998).

Classes of wounds

Wounds are classified as closed or open wounds depending on the underlying source of wound genesis and as acute or chronic wounds based on wound healing physiology (Matadeen *et al.*, 2014; Yogesh *et al.*, 2013; Shivani *et al.*, 2012).

Open wounds and closed wounds

Open wounds cause blood to flow out from the body alongside noticeable hemorrhage. In contrast, a closed wound causes blood to flow out of the circulatory system but lingers in the body, resulting in confusion. (Table 1).

Table 1: Classification of wounds (Open wounds and closed) (Györgyi, 2016; Yogesh *et al.*, 2013; Shivani *et al.*, 2012)

S/N	Wounds	Kind of wound	Causes	Injury causes
1	Bruise (Contusion)	Closed	Blow from something blunt	Damage tissue under the skin
2	Hematomas or blood tumor	Closed	Damage to a blood vessel	causes blood to collect under the skin
3	Crush injury	Closed	Application of great force on the skin for an extended period	causes blood to collect under the skin
4	Puncture wounds	Open	Blunt or sharp-pointed instruments such as needle or nail	Skin and underlying tissue damage and possible infection because dirt can easily cross into the wound depth
5	Laceration wounds	Open	Machinery, barbed wire, teeth or claws	Skin and underlying Tissue loss damage
6	Tear wounds	Open	Severe force or teeth	Skin and other soft tissues to be partially or completely

				torn away
7	Abrasions wounds	Open	Skin being scraped across a rough and or hard surface	The outer layer of skin is scraped off that revealed nerve endings leading to loss of blood similar to a burn and a painful injury
8	Gunshot wounds	Open	a bullet or similar projectile driving into the body	Blood and tissue loss

Acute wounds

Acute wounds are described as tissue injuries treated in a systematic and timely manner, resulting in the restoration of anatomical and functional integrity. Cuts are the most common cause of acute wounds, and the repairing phase is typically completed within a reasonable time frame (Yogesh *et al.*, 2013; Shivani *et al.*, 2012).

Chronic wounds

Chronic wounds do not heal normally and cause pathologic discomfort as a result. Chronic wounds are the chief root of physical disability and either take a long time to repair, don't heal, or return regularly (Menke *et al.*, 2007). A clean and uninfected surgical incisional wound approximated by surgical sutures is an example of a chronic wound (Yogesh *et al.*, 2013; Shivani *et al.*, 2012; Menke *et al.*, 2007; Jie *et al.*, 2007). Ablation, antibiotics, tissue implantations, and proteolytic enzymes are some of the latest methods for treating chronic wounds. However, they all have downsides and severe side effects (Chitra *et al.*, 2009).

Mechanism of Wound Healing

Wound healing can be defined as a complex process, with the wound environment fluctuating with the shifting health status of a person (Heather *et al.*, 2011). In a normal phenomenon, the outmost and the innermost layer of the skin occurs in steady-state equilibrium. It forms a shielding wall contrary to the external environment, which instantaneously instigates the usual pathophysiological mechanism of wound healing when broken due to injury. When the skin is injured, complex biochemical reactions occur in a well-ordered sequence to repair the damage. Platelets clump together at the injury site to produce a fibrin clot a few seconds just after the injury. This clot helps to control aggressive bleeding and achieve haemostasis. This all-encompassing healing process, which begins as

soon as an injury occurs, might linger for the donkey months or years (Lazarus *et al.*, 1994). **Figure 1.** Described the uninterrupted, overlapping, and precisely programmed three phases of the wound healing process: inflammation, proliferation, and tissue remodeling (Shivananda *et al.*, 2009; Jie *et al.*, 2007).

- **Inflammatory phase:** This phase begins instantly after the wound and generally lasts for about 24 and 48 hours and may continue for about two weeks. The inflammatory stage unveils the haemostatic systems that instantaneously stop blood loss at the wound site (Yogesh *et al.*, 2013; Jie *et al.*, 2007). This hemostasis mechanism is the first step in the inflammatory phase. It consists of two major processes: developing a fibrin clot and coagulation (Jie *et al.*, 2007), which commences straightaway after wounding, with vascular constriction and fibrin clot creation. Then, proinflammatory cytokine and growth factors such as transforming growth factor, platelet-derived growth factor, fibroblast growth factor, and epidermal growth factor are released by both the clot and the underlying wound tissue (Yolanda *et al.*, 2014; Guo and DiPietro, 2010).

- **Proliferative phase:** This is the second phase of wound healing and usually persists up to two days to twenty-one days after the first phase (Yogesh *et al.*, 2013). Angiogenesis, collagen installation, granulation tissue growth, epithelialization, and wound shrinking are all characteristics of this phase. Angiogenesis is the formation of new blood vessels from endothelial cells. Fibroblasts develop and generate a fresh, ephemeral extracellular matrix by releasing collagen and fibronectin during fibroplasia and granulation tissue formation. Collagens, the key components that reinforce and sustain extracellular tissue, include large amounts of hydroxyproline, a biomarker for tissue protein. Epithelial cells multiply and disseminate across the wound site during epithelialization. The wound margins move closer to the wound center as the myofibroblasts shrink, causing the wound boundaries to constrict (Yogesh *et al.*, 2013; Shivananda *et al.*, 2009).

- **Remodeling phase:** This phase continues for about twenty-one days to two years. Fresh collagen is forged at this stage. One of the critical features of the remodeling phase is Extracellular matrix remodeling to an architecture that approaches that of the normal tissue (Jie *et al.*, 2007; Guo and DiPietro, 2010). Type III collagen (which is prevalent during proliferation) becomes gradually degraded and replaced by type I collagen during this phase. And thus, the realignment of collagen tissue takes place, and the intermolecular cross-linking of collagen caused by vitamin C-dependent hydroxylation increases tissue breaking strength (Yolanda *et al.*, 2014; Yogesh *et al.*, 2013). As a result, the scar smoothness and tissues become 80 percent tougher than the original tissue (Yogesh *et al.*,

2013). According to Guo and DiPietro, 2010, many factors can impaired wound healing, and these factors that cause impairment can be classified into local and systemic. Local factors (temperature, oxygenation, infection, foreign body, and venous sufficiency) directly influence the characteristics of the wound itself. In contrast, systemic factors (age, gender, sex hormones, stress, hereditary healing, Obesity, medications: (glucocorticoid steroids, non-steroidal anti-inflammatory drugs, chemotherapy, alcoholism, and smoking), immunocompromised conditions such as cancer, radiation therapy, improper diet) are the individual's overall health or ailment condition that inhibits his or her capacity to recuperate (Guo and DiPietro, 2010).

Figure 1: Stages of the wound healing process.

Roles of phytochemical in wound healing

The healing of a wound as a process is a natural occurrence by which the body overcomes damage to the tissue. However, the healing pace is slow, and the probability of microbial septicity is very high. This calls for the great request of substance that accelerates the healing process (Sherratt & Dallon, 2002). Phytochemicals are bioactive compounds that occur naturally in plants as secondary metabolites that work with nutrients to protect against pathogenic attack, and research has demonstrated its protective effects against various diseases (Opawale *et al.*, 2017; Altiok, 2010). Some of the biological properties of these secondary metabolites include antioxidant activities, antimicrobial effects, stimulation of the immune system, astringent and anticancer properties (Altiok, 2010). Though phytochemicals are not vital nutrients and are not necessary by the human body for sustaining life, but

have important properties to avert or fight some diseases (Emmanuel *et al.*, 2014). Phytochemicals are classified as tannins, alkaloids, terpenoids, phenolic compounds, flavonoids, glycosides, saponins, anthraquinones, and so on (Altiook, 2010). **Figure 2.** Summarized the key function of phytoconstituents like triterpenoids, alkaloids, and flavonoids in the process of wound healing because of their astringent and antimicrobial properties, which are thought to contribute to wound closure (contraction) and an increment in epithelialization rate (Emmanuel *et al.*, 2014). Narendhirakannan *et al.*, 2012 also stated that tannins, phenols, and flavonoids could be answerable for healing owing to their antioxidant properties. An increase in total antioxidant status has been essential in recovery from wounds (Narendhirakannan *et al.*, 2012).

Figure 2: Roles of phytochemicals in wound healing

4.0 Medicinal plants with reported wound-healing activities

As shown in **Figure 3**, different medicinal plant parts as wound healers have received serious attention in the science community, and several medicinal plants from Africa with scientifically proven wound-healing activities are reported in this section.

Figure 3: Different parts of the medicinal plant as a wound healer.

Morinda citrifolia

Morinda citrifolia is a traditional Polynesian medicinal herb. The leaf extracts appear to be the chief aboriginal use as a topical therapeutic agent for wound healing. The wound-healing activity of the ethanolic extract of noni leaves (150 mg/kg/day) was evaluated in rats using excision. When compared to controls, the extract showed a 92.45 percent diminution in wound area (Hai *et al.*, 2020), which is far better than the research accomplished by the Nyak group of researchers in 2007, which showed a 71 percent decrease in wound area by the *Morinda citrifolia* ethanolic leaf when compared to a control of 57 percent. In addition, noni-treated animals had considerably higher granulation tissue weight and hydroxyproline concentration in dead space wounds relative to controls. Noni leaf extract appears to help wound healing by accelerating wound contraction, shortening epithelialization time, elevating hydroxyproline content, and enhancing histological features (Hai *et al.*, 2020; Nyak *et al.*, 2007).

Plumbago zeylanica

Plumbago zeylanica belonging to the family *Plumbaginaceae* has been reported to be employed by the majority of the prehistoric people primarily for wound healing activity, among other issues and the Kodati team in 2011 evaluated the wound healing potential of this plant to further emphasize its pharmacology and phytochemistry. Their findings reveal that the methanolic root extract of *Plumbago zeylanica* has remarkable wound healing activity

in rats, with a 100 percent wound healing rate compared to the control, which is 80.64 percent. The wound-healing action of methanolic root extracts of *Plumbago zeylanica*, according to the Kodati research team, could be attributed to the presence of bioactive compound reported in **Table 2**. (Kodati *et al.*, 2011)

Kigelia africana

Kigelia africana is an excellent medicinal plant employed to alleviate fungal infestations, psoriatic arthritis, dermatitis, and cancer (Agyare *et al.*, 2013). Kigelinone, vernolic acid, kigelin, iridoids, luteolin, and 6-hydroxyluteolin have been detected in the root, wood, and leaf of this plant. In comparison to untreated wound tissues, extract-treated wound tissues exhibited better collaboration, re-epithelialization, and fast granulation development. As shown in **Table 2**, from the result of the study carried out by the Agyare research team in 2013, leaves and roots methanolic extract of *Kigelia Africana* was found to give 100% healing rate when compared with the control, which gave 96.59% on the last day of the experiment (Agyare *et al.*, 2013)

Strophanthus hispidus

Strophanthus hispidus belonging to the family *Apocynaceae* is used as an antidote to poison and to combat skin ailments such as fungal infestations, psoriatic arthritis, dermatitis, and cancer, boils, leprosy, syphilis, as well as cancer (Ayoola *et al.*, 2008; Agyare *et al.*, 2013). Powerful antioxidant and antimicrobial bioactive compounds have been reported to be present in the root, wood, and leaf (Agyare *et al.*, 2013). Extract-treated wound tissues showed improved collagenation, re-epithelialization, and granulation growth compared to untreated wound tissues (Ayoola *et al.*, 2008). As shown in **Table 2**, from the result of the study carried out by Agyare *et al.* in 2013, leaves and roots methanolic extract of *Strophanthus hispidus* was found to contain important phytochemicals which are responsible for the 100% healing rate of the extract when compared with the control which gave 96.59% on the last day of the experiment.

Aspilia africana

Aspilia Africana, a common weed of filed crop in the forest region, is one of the many indigenous plants used in folk medicine to curb certain illnesses such as rheumatic pain, anticoagulating activities, anti-malaria, and so on and was found to contain vital phytochemicals such as Alkaloids (most prominent), Saponins, Flavonoids, Tannins, Phenols (the lowest) as well as vitamins (Abii and Onuoha, 2011; Osunwoke *et al.*, 2014). Furthermore, from the result of the research done by Osunwoke and his coworkers in the year 2013, it was evident that the aqueous

extracts of the leave of *Aspilia africana* promotes wound healing activity through increased inflammatory response and neovascularization with a recovery rate of 82.21%, as compared to the untreated group with 52.84%.

Swietenia macrophylla

Swietenia macrophylla is a well-known medicinal herb. Duravi research team previously reported on the phytochemical screening and antimicrobial activity of leaf, seed, and fruit in 2016. The phytochemical assays indicated the presence of prevalent phytocompounds like alkaloids, flavonoids, tannins, terpenoids, glycosides, saponins, volatile oils, amino acids, and proteins as principal active constituents, and the seed extract had huge anti-proliferative effects on bacterial and fungal replication and growth (Duravi *et al.*, 2016). In 2017, the Kiran research group investigated the tissue regeneration ability of an ethanolic extract of *Swietenia macrophylla* seeds ointment in an excision wound model using a white rat. In terms of wound contraction ability, wound closure time, and epithelialization period, the extract ointments worked fairly well in the excision wound model as the group treated with conventional medicine Betadine ointment and the control group. The proposal that *Swietenia macrophylla* seed extract demonstrates considerable wound healing was also supported by histological investigation. *Swietenia macrophylla* has been discovered to have remarkable wound-healing abilities. This was demonstrated by reducing wound closure and epithelialization time (Kiran *et al.*, 2017).

Azadirachta indica

Azadirachta indica (Neem tree) of *Meliaceae* family is an evergreen tree that is prevalent in Asia but has now grown in Western Africa region and has been confirmed to contain important phytochemicals such as Alkaloids, Flavonoids, Glycosides, Reducing sugar, Polysaccharides, Phytosterols, Steroids, Phenols, Saponins, Tannins (Subramanian, 2018; Sushree *et al.*, 2017; Osunwoke *et al.*, 2013). The aqueous leaf extract of *Azadirachta indica* was shown to have a notably higher rate of wound contraction in the treatment group than the reference group in a study conducted by Osunwoke *et al.* in 2013 excision wound design. Furthermore, in both excision and incision wound models, a methanolic extract of the leaf and stem bark of *Azadirachta indica* cream has proven to enhance wound-healing activities, and its oil has been found to boosts wound tensile strength and wound closure rate, according to (Barua *et al.*, 2010; Maan *et al.*, 2010; Pandey *et al.*, 2012).

Mallotus oppositifolius

Mallotus oppositifolius is called *Nyanyafurowa* by the Ghananians and *Ukpo* in Nigeria. Tapeworms and diarrhea have both been medicated with a leaf and stalk peel infusion. To relieve pain, crushed or chewed raw leaf blended with butter is applied to injuries and blisters and rheumatism, dermatitis, and burns sometimes blended with butter. Decoction of the leaves is used for the management of headaches, epilepsy, or mental illness. The crushed leaves or leaf sap are applied to aching teeth and inflamed eyes (Agyare *et al.*, 2014). In a study conducted by Agyare *et al.*, methanolic leaf extract of *Mallotus oppositifolius* produced a considerable inflammatory response, fibrosis, and collagenation in an excision wound model (Agyare *et al.*, 2014).

Momordica charantia

Momordica charantia, a member of the *Curcubitaceae* family, is also famously known as bitter gourd, bitter lemon, and Nyanya in Ghana. The plant has historically been used to heal wounds, ulcerative colitis, malaria, hemorrhoids, dermatitis, parasitic infections, and yaws (Burkill, 2000). Agyare *et al.* reported the wound-healing efficacy of *Momordica charantia* in 2014, adopting an excision wound model. When the treated wound tissue was compared to the untreated wound tissue, the methanolic leaf extract of the plant demonstrated considerable wound closure. In contrast, histological examination of the wound tissues revealed strong fibrosis and collagenation (Agyare *et al.*, 2014).

Tridax procumbens

The plant *Tridax procumbens* is popularly referred to as "coat buttons." The effects of whole plant extract, aqueous and ethanolic extract of *Tridax procumbens* on lysyl oxidase activity, protein and nucleic acid contents, and tensile strength, all of which are essential for wound healing, have been documented in the literature, with a large increase in animals treated with aqueous and ethanolic extract fractions compared to the untreated in diverse wound healing simulations (Alankar *et al.*, 2020; Yaduvanshi *et al.*, 2011). Excision wounds treated with extract of the juice of *Tridax procumbens* (1 mg/g) showed a considerable rise in collagen production of 38.81 percent in comparison to vehicle-treated wounds, according to Yaduvanshi *et al.*, 2011. In cutaneous wounds treated with *Tridax procumbens* juice extract, histopathological analyses revealed enhanced infiltration of proinflammatory cells, fibroblast proliferation, and re-epithelialization with mild vascularity. Dermal wounds treated with *Tridax procumbens* juice extract at a dose of 4 mg/g, on the other hand, produced inflammation, oedematous tissue, and impaired vascularity (Alankar *et al.*, 2020; Yaduvanshi *et al.*, 2011)

Crinum jagus

Crinum jagus belonging to *Lilliaceae* family, is a tender perennial bulb with tulip-like (showy) white flowers and called Bush onions, and it's found in tropical and subtropical areas all over the world (Udegbumam *et al.*, 2015). The study of Udegbumam *et al.*, in 2015 have established that the wound healing of *Crinum jagus* extract partly increasing collagen deposition and epithelialization, and the extract elicited the best wound healing activity at a concentration of 10%, and the activity was concentration-dependent. They (Udegbumam *et al.*, 2015) suggested that the wound healing potentials of the extract could be attributed to the presence of polyphenolic compounds, including tannins, saponins, glycosides, and alkaloids in the extract.

Bridelia ferruginea

Bridelia ferruginea of the genus *Bridelia* belonging to the family of *Euphorbiaceae* is a savannah species commonly called Kirni, Kizni in Hausa language, Marehi in Fulani language, Iralodan in Yoruba language and Ola in Igbo language (Abdullahi *et al.*, 2019; Kolawale *et al.*, 2007). Ethnobotanically, the bark, leaf, and fruit have been used to treat abrasions, boils, burns, wound, skin infection, gastrointestinal problems, diabetes, cystitis, ulcerative colitis, cough, genital herpes, communicable diseases, including sexually transmitted infections, cancer, and it is also a remedy for toxin (Abdullahi *et al.*, 2019). From the experimental research carried out by Ezike *et al.*, in the year 2019 and Udegbumam *et al.*, 2011, the ethanolic leaf extract and methanolic stem bark extract of *Bridelia ferruginea* have been reported to significantly enhanced 100% wound contraction and epithelialization. In addition, the plant extract (1 to 30 g/mL) has been proven to have an appreciable impact on cutaneous fibroblast growth (Adetutu *et al.*, 2011). The ethnobotanical therapeutic action of this plant is possibly a result of important bioactive chemicals such as Alkaloids, Carbohydrates, Flavanoids, Cardiac glycosides, Saponins, Steroids, Tannin, Fat, and Oil that are present in all parts of the plant as reported from the phytochemical screening study carried out by Abdullahi *et al.*, 2019.

Radix paeoniae

Radix paeoniae (*Paeonaceae*) is used to reduce pain and treat amenorrhea, painful injuries, hemoptysis, inflammation, furuncle, and ulcers (Xing *et al.*, 2004). Excision, incision, and dead space wound models on Wistar rats were used to test aqueous extracts of *Radix paeoniae* roots for wound healing. In addition, tissue breaking strength, epithelialization, wound contraction, and granulation tissue dry weight were investigated. Compared to

the Nitrofurazone ointment-treated control group, the test group showed considerable wound-healing efficiency (Malviya and Jain, 2009).

Hibiscus rosa sinensis

Hibiscus rosa sinensis belonging to *Malvaceae* family is an indigenous tropical and sub-tropical plant (Kumar and Singh, 2012) that has been used conventionally for the management of a wide range of diseases which includes promotion of wound healing and some other biological activities such as antihypertensive, antitumor, antioxidant, and so on. In rats, ethanolic leaf extract (120 milligrams per kilogram per day) reduced wound area by 86 percent compared to controls (75 percent decrease). Similarly, the extract-treated rats had comparatively stronger skin breaking strength and epithelialization than the controls (Bhaskar and Nithya, 2012). In addition, granulation tissue dry and wet weight and hydroxyproline level were documented to have increased significantly compared with controls. Bhaskar and Nithya used excision, incision, and dead space wound models to investigate the effects of an ethanolic extract of *Hibiscus rosa s.* flowers on Wistar rat. As indicated by rises in DNA, total protein, and total collagen content of granulation tissues, the extract boosted cell growth and collagen formation at the injury site. Furthermore, compared to the control, the extract facilitated wound healing drastically, as revealed by better epithelialization and wound contraction rates and higher wound tensile strength, and wet and dry granulation tissue weights (Bhaskar and Nithya, 2012).

Alternanthera sessilis

Alternanthera sessilis belonging to the *Amaranthaceae* family of plants is historically used to treat ulceration, lesions, wounds, fevers, ophthalmia, gonorrhea, skin rash, burning sensations, dysentery, indigestion, skin liver and spleen ailments (Kannan *et al.*, 2014; Hossain *et al.*, 2014). Previously, the wound-healing activity of *Alternanthera sessilis* was carried out by Jalalpure *et al.* 2008. The oral administration of the plant's chloroform leaf extract at a 200 mg/kg body weight dose resulted in a vastly reduced wound area and improved re-epithelialization in rats. Meanwhile, the scar size following full epithelialization was revealed to be 33.2 ± 0.7 mm² in the excision wound model, with wound breaking strength of 388 ± 5.85 gram in the incision wound model, and granuloma dry weight of 47.7 ± 2.29 gram and granuloma breaking strength of 247 ± 10.2 gram in granuloma analyses (Jalalpure *et al.* 2008).

Table 2: Summary of some medicinal plants with wound healing activity

Plant	Part used (Extract)	Phytochemical present	Route	HWC/HSBS (%/g)		References
				Extract	Control	
<i>Morinda citrifolia</i>	Leaf (Ethanolic)	Flavonoids, alkaloids, tannins, triterpenes, saponins, coumarins, anthraquinones, carotenoids, organic acids, reducing agents	Topical	92.45	54.46	Hai <i>et al.</i> , 2020; Nyak <i>et al.</i> , 2007
<i>Plumbago zeylanica</i> L.	Root (Methanolic)	Alkaloids, Carbohydrates, Flavanoids, Glycosides, Saponins, Steroids, Tannin	Topical	100	80.64	Kodati <i>et al.</i> , 2011
<i>Kigelia Africana</i>	Leaf (Methanolic)	Saponins, Flavonoids, Steroids, Carbohydrate, Sapogenetic glycosides, Tannins	Topical	100	96.59	Agyare <i>et al.</i> , 2013
<i>Kigelia Africana</i>	Stem bark (Methanolic)	Saponins, Steroids, Carbohydrate, Sapogenetic glycosides, Tannins	Topical	100	96.59	Agyare <i>et al.</i> , 2013
<i>Strophanthus hispidus</i>	Root (Methanolic)	Alkaloids, Saponins, Steroids, Carbohydrate, Sapogenetic glycosides, Tannins	Topical	100	96.59	Ayoola <i>et al.</i> , 2008; Agyare <i>et al.</i> , 2013

<i>Strophanthus hispidus</i>	Leaf (Methanolic)	Alkaloids, Flavonoids, Saponins, Steroids, Carbohydrate, Sapogenetic glycosides, Tannins	Topical	100	96.59	Ayoola <i>et al.</i> , 2008; Agyare <i>et al.</i> , 2013
<i>Aspilia Africana</i>	Leaf (Water)	Alkaloids, Saponins, Flavonoids, Tannins, Phenols	Topical	82.21	52.84	Abii and Onuoha, 2011; Osunwoke <i>et al.</i> , 2014
<i>Swietenia macrophylla</i>	Seed (Methanolic)	Alkaloids, Tannins, Steroids, Flavonoids, Saponins, Carbohydrate, Amino acids, Oil	Topical	100	85.00	Kiran <i>et al.</i> , 2017; Durai and Geetha, 2016
<i>Azadirachta indica</i>	Leaf (Aqueous)	Alkaloids, Flavonoids, Glycosides, Reducing sugar, Polysaccharides, Phytosterols, Phenols, Saponins, Tannins	Topical	92.20	85.19	Subramanian, 2018; Sushree <i>et al.</i> , 2017; Osunwoke <i>et al.</i> , 2013; Barua <i>et al.</i> , 2010; Pandey <i>et al.</i> , 2012
<i>Azadirachta indica</i>	Stem bark (Ethanolic)	Alkaloids, Flavonoids, Glycosides, Reducing sugar, Steroids, Phenols, Saponins, Tannins	Topical	79.39 240.4g	78 148g	Maan <i>et al.</i> , 2010
<i>Mallotus oppositifolius</i>	Leaf (Methanolic)	Alkaloids, Tannins, Flavonoids, Glycosides	Topical	71.84	73.04	Agyare <i>et al.</i> , 2014
<i>Momordica charantia</i>	Leaf (Methanolic)	Alkaloids, Tannins, Flavonoids, Glycosides, Saponins	Topical	69.84	73.04	Burkill, 2000; Agyare <i>et al.</i> , 2014

<i>Tridax procumbens</i>	Leaf (Ethanolic and Aqueous)	Proteins, Amino acids, Flavonoids, Carbohydrate, Glycosides, Tannins	Oral	100.00	92.30	Alankar <i>et al.</i> , 2020; Yaduvanshi <i>et al.</i> , 2011
<i>Crinum jagus</i>	Bulbs (Methanolic)	Alkaloids, Tannins, Flavonoids, Glycosides, Saponins	Topical	99.60 344.48g	97.14 224.46g	Udegbumam <i>et al.</i> , 2015
<i>Bridelia ferruginea</i>	Leaf (Ethanolic)	Alkaloids, Carbohydrates, Flavanoids, Cardiac glycosides, Saponins, Steroids, Tannin, Fat and Oil	Topical	100.00	80.90	Abdullahi <i>et al.</i> , 2019; Ezike <i>et al.</i> , 2015 Adetutu <i>et al.</i> , 2011; Udeegbumam <i>et al.</i> , 2011; Kolawale <i>et al.</i> , 2007
<i>Bridelia ferruginea</i>	Stem barks (Methanolic)	Alkaloids, Carbohydrates, Flavanoids, Cardiac glycosides, Saponins, Terpenoids, Tannin, Fat and Oil	Topical	100.00	95.97	Abdullahi <i>et al.</i> , 2019; Ezike <i>et al.</i> , 2015
<i>Radix paeoniae</i>	Root (Aqueous)	Alkaloids, Carbohydrates, Flavanoids, glycosides, Tannins, Resins, Terpenoids	Topical	97.69 420.33g	63.84 277.86g	Malviya and Jain, 2009; Xing <i>et al.</i> , 2004
<i>Hibiscus rosa sinensis</i>	Flowers (Ethanolic)	Alkaloids, Phytosterol, Flavanoids, Saponins, Tannins, Phenolics compounds	Topical	100.00	60.10	Kumar and Singh, 2012; Bhaskar and Nithya, 2012

<i>Alternanthera</i>	Leaves	Carbohydrates, Phenols, phytosterol,	Oral	97.40	90.20	Kannan <i>et al.</i> , 2014; Hossain <i>et al.</i> , 2014;
<i>sessilis</i>	(Chloroform)	Tannins,				Jalalpure <i>et al.</i> 2008

HWC: Highest wound closure in percent; **HSBS:** Highest skin breaking strength in gram

5.0 Recent development on the use of plants for medicinal purpose

In recent times, researchers have focused more on combining the strength of modern days' scientific techniques such as FTIR, GS-MS, and NMR to identify the key architects of phytoconstituents.

Also, other minor metabolites are being harnessed by researchers in recent times to further campaign the importance of medicinal plants in the health care system. Furthermore, agreement between oral and topical use of the medicinal plant has gained the full interest of many chemists nowadays to further understand the chief working mechanism of medicinal plant in the body.

6.0 Future work and research direction

It is glaring that artificial intelligence (AI), including machine learning and deep learning, has not been fully deployed into computer-aided drug design (CADD) and bioactive compound identification in the plant extract. Thus, effort must be channeled in this direction.

A variation in the chemo-taxonomical balance of the phytochemicals in the plant as caused by changes in the environment could pose an inherent enervating danger to honorable consumerists of the plant extracts. Hence, maiden biosafety tests should be done before the administration of the plant extracts for therapeutic purposes and find a way to safeguard biodiversity to prevent the prominent plants of medicinal value from being defunct. In addition, a well-designed clinical evaluation needs to be worked upon. Serious work should be done on the LD₅₀ dose-response concentration that might cause side effects like epidermal degeneration. Researchers could probe the isolated bioactive compound responsible for the wound-healing activity separately to develop wound healing drugs with sound therapeutic value. Also, trial research should be done in combining/extracting two or more medicinal plants together to treat wounds because this will increase the probability of having all the key phytochemicals responsible for wound healing in a reasonable quantity in one formulation.

Conclusion

A mini-review of the wound-healing potential of medicinal plants has been carried out in this study. Wound healing is a biochemical process that starts with damage and ends with the creation of scar tissue. The chief aim of wound management is to prevent susceptibility factors that inhibit wound healing (for example, poor diet, infection at the wound site, diabetes), enhance the healing process, and reduce the incidence of wound contagions. This review has

shown that medicinal plant plays a chief role in meeting the unbeatable goals of wound management, and thus, cannot be overlooked at any point in time no matter how. Over the years, medicinal plants have been used in folk medicine as topical and oral preparations to know the roles of phytochemicals in wound healing to promote wound care and healing activities. This review also suggested that these plants possibly owe their wound healing processes to the antimicrobial, astringent, anti-inflammatory, and antioxidant properties combined with the various phytochemicals present. Also, from this review, we can conclude that the most widely used method of application of extract formulation is topical. In most cases, only the wound closure rate is commonly and frequently assessed, unlike the skin breaking strength after or during the healing period.

Declaration of Conflict of Interests

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